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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SALMON, KATHERINE D	
ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 11/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/724,837	SUZUKI ET AL.	
	Examiner	Art Unit	
	Katherine Salmon	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 September 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This action is in response to the papers filed 9/12/2006. Currently, Claims 1-9 are pending.

2. The following objections and rejections are newly applied, as necessitated by amendment. Response to arguments follows.

3. This action is FINAL

Withdrawn Objections

4. The claim objections made in Section 1 of the previous office action are moot in view of the amendments to the claims.

Withdrawn Rejections

5. The rejection of Claims 1-9 under 35 USC 112/2nd paragraph made in section 2 of the previous office action, is moot in view of the amendments to the claims.

6. The rejection of Claim 1 under 35 USC 103(a) made in section 4 of the previous office action, is moot in view of the amendments to the claims. Specifically, the addition of removing ribosomal RNA prior to mRNA.

7. The rejection of Claims 2-3 under 35 USC 103(a) made in section 5 of the previous office action, is moot in view of the amendments to the claims. Specifically, the addition of removing ribosomal RNA prior to mRNA.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

In order to efficiently describe the art rejections presented the examiner has labeled each step of Claim 1 in order to make the art rejection easier to follow.

CLAIM 1: 1A: an mRNA isolation process for isolating an mRNA from a prokaryotic cell after removing rRNA.

1B: a polyA addition process for adding a polyA at the 3' end of the mRNA

1C: a cDNA synthesis process for synthesizing a cDNA from the polyA-added mRNA

1D: a cDNA processing process for preparing an adaptor attached cDNA fragment having the sequence of the first adapter at one end and the sequence of a second adapter at the other end

1E: a first PCR process for performing PCR with the adaptor-attached cDNA fragments, using a first primer having a sequence complementary to the sequence of the first adaptor and a second primer having a sequence complementary to the sequence of the second adaptor

1F: an electrophoresis process

1G: a cDNA fragment recovery process

9. Claims 1-3 are rejected under 35 U.S.C. 103(a) as being unpatentable over Weissman et al. (US Patent 5712126 January 27, 1998) in view of Wendisch et al. (Analytical Biochemistry 2001 Vol. 290 p. 205), and Murphy et al. (US Patent Application Publication 2003/0175709).

Weissman et al. teaches a method to analyze gene expression by selective PCR amplification and display of 3'end restriction fragments of double stranded cDNAs (Abstract). With regard to Claim 1C, Weissman et al. teaches cDNA synthesis from a polyA tailed mRNA (Figure 1 step 1). With regard to Claim 1D, Weissman et al. teaches a cDNA with a first and second adapter attaches (Figure 1, steps 4 and 5). With regard to Claim 1E, Weissman et al. teaches a PCR cycling method (Figure 1 step 6). Weissman et al. teaches two primers attached to the first and second adapters (Figure

1, Step 5). With regard to Claim 1F, Weissman et al. teaches the PCR products were analyzed on a 6% polyacrylamide sequencing gel (Column 5, lines 60-62). With regard to Claim 1G, Weissman et al. teaches cDNA fragment was recovered by cutting by a single or multiple restriction enzymes, extracting the bands from the display gel, and subcloning into a pCRscript to obtain plasmids (Column 6, lines 5-10).

Weissman et al., however, does not teach a method of removing rRNA from total RNA to enrich mRNA or adding a polyA tail to mRNA from a prokaryotic gene (Claim 1A and B).

Murphy et al. teaches s a method of enriching mRNA (Abstract). With regard to Claim 1A, Murphy et al. teaches the depletion (removal) of rRNA from a sample (p. 5 paragraph 30). Murphy et al. teaches the depletion of rRNA is a way of enriching the mRNA such that mRNA can be used to prepare cDNA (p. 5 paragraph 31).

With regard to Claim 2, Murphy et al. teaches a method of hybridizing two polynucleotides (one to the 16S region and one to the 23S region) to deplete rRNA from prokaryotic total RNA (p. 22 Example 2 paragraph 200). Murphy et al. teaches adding a tag substance to each to the polynucleotides in the form of an oligo (dT) MagBead (p. 22 paragraph 203). This bead is the tag attached to a stretch of Ts which would attach to the stretch of As on each of the oligonucleotides (p. 21-22 list of potential oligonucleotides for 16S and 23S and p. 22 paragraph 203). Murphy et al. teaches the bridging nucleic acid in which a portion hybridizes to a polynucleotide with a bead attaches and a portion to the targeted nucleic acid (16s, 23s regions) (Figure 1).

Murphy et al. teaches removing the rRNA using the magnetic bead (p. 22 paragraph 203-206).

With regard to Claim 3, Murphy et al. teaches that any region of 5 contiguous base pairs may be used therefore many different regions of the target can be hybridized with one bridging nucleic acid (p. 8 paragraph 53 1st column). Murphy et al. teaches the bridging nucleic acid can be comprised of up to 2 or more targeting regions (p. 3 paragraph 16). Therefore, Murphy et al. teaches using a bridging nucleic acid that is comprised of at least 5 nucleotides and would hybridize to both regions of the 16S and 23S.

Wendisch et al. teaches a method to add polyadenylate (polyA) to extracted E. Coli (prokaryote) (Abstract). With regard to Claim 1A, Wendisch et al. teaches isolating a population of cellular mRNAs in crude cell extracts by mechanical lysis (p. 205 2nd column last paragraph last full sentience). With regard to Claim 1B, Wendisch et al. teaches the mRNA was polyadenylated with poly(a) polymerase I (p. 205 2nd column last full sentence).

Therefore it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Weissman et al. to use polyA-prokaryotic mRNA as taught by Wendisch et al. The ordinary artisan would have been motivated to modify the method of Weissman et al. to use polyA-prokaryotic mRNA because Wendisch et al. teaches that bacterial mRNAs are not uniformly polyadenylated and cannot be distinguished from rRNA or tRNA (p. 205 2nd column 1st line 2nd paragraph). Wendisch et al. teaches that polyadenylated RNA will increase the

signal intensities in gene expression studies because the mRNA is enriched (p. 213 last paragraph). The ordinary artisan would want to enrich the mRNA in order to produce sufficient signal intensity for gene expression studies. The ordinary artisan would have been motivated to remove rRNA prior to the attachment of the polyA tail as taught by Murphy et al. because Murphy et al. teaches a method of improved mRNA enrichment prior to polyadenylation in order to reduce the amount of RNA needed to use mRNA in expression assays (p. 1-2 paragraphs 6 and 10).

Response to Arguments

The response asserts Wendisch et al. does not teach removing rRNA from total RNA prior to adding the polyA tail to the mRNA (p. 8 last paragraph). The response has been fully considered but is not found persuasive. The combination of Weissman et al., Wendisch et al., and Murphy et al. teach the method as claimed. Weissman et al. teaches all the limiting steps to make cDNA from mRNA. Weissman et al. teaches the attachment of polyA to prokaryotic cells. Murphy et al. teaches a method of depleting rRNA prior to using mRNA by attaching magnetic beads to oligonucleotides of 16S and 23S regions and removing the rRNA from solution.

10. Claims 4-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Weissman et al. (US Patent 5712126 January 27, 1998) in view of Wendisch et al. (Analytical Biochemistry 2001 Vol. 290 p. 205), and Murphy et al. (US Patent Application Publication 2003/0175709) as applied to claims 1 above, and further in view of Belyavsky et al. (US Patent 6120996 September 19, 2000).

Neither Weissman et al., Wendisch et al., or Murphy et al. teach a process of cDNA synthesis with a tag substance, restriction enzymes, and a high-affinity substance, or using markers on both primers, a second PCR after cDNA recovery, or cutting out the gel to litigate and clone in E. Coli.

Belyavsky et al. teaches a method of identification of differentially expressed mRNA which consists of synthesizing from a set of sequences of mRNA sets of fragments of complementary cDNA that are separated and differential signal intensity is identified (Abstract). With regard to Claim 4 and 7, Belyavsky et al. teaches attaching a 5' biotin group to the cDNA and is bonded to a streptavidin-containing solid support (column 5 lines 1-5 and 15-18). Belyavsky et al. teaches cleaving the cDNA with a restriction enzyme such as Sau3A (Type 1 Restriction enzyme) (Column 5, lines 10-15). Belyavsky et al. teaches amplifying the fragments of cDNA by means of a PCR with a primer that is in the adaptor and modified with a biotin group (Column 5, lines 20-24). With regard to Claim 6, Belyavsky et al. teaches a label is added to the 3' primer (Column 5 lines 27-30), therefore Belyavsky et al. teaches a biotin label on one primer and a radioactive label on the other primer. Belyavsky et al. teaches the cDNA goes through sequential exhaustive cleavage with 8-10 restrictions carried out with restriction of 6-letter, 5-letter, and 4-letter restriction sites (Column 5 lines 35-40). Belyavsky et al. teaches that cleavage is done with EcoRV (type II restriction enzyme) (Column 8 lines 40-45). Belyavsky et al. teaches the labeled fragments are release and separated (Column 5, lines 35-45). Belyavsky et al. teaches the cDNA fragment is eluted from the gel and is amplified by means of PCR using adapter primers (Column 6, lines 9-12).

With regard to Claim 5, Belyavsky et al. teaches that the fragments are cut out of the gel and eluted by incubation (Column 8, lines 54-56). Belyavsky et al. teaches the amplified fragment is cloned into a plasmid or phage vector (Column 6, lines 15-18). With regard to Claim 8, Belyavsky et al. teaches the amplified fragment is ligated to plasmid vector pUC18 (an e.coli phagemid) (Column 8, line 67 and Column 9 line 1).

Therefore it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Weissman et al. and Wendisch et al. to incorporate a process of cDNA synthesis with a tag substance, restriction enzymes, and a high-affinity substance, or using markers on both primers, a second PCR after cDNA recovery, or cutting out the gel to litigate and clone in E. Coli as taught by Belyavsky et al. The ordinary artisan would have been motivated to modify the method of Weissman et al. and Wendisch et al. to incorporate a process of cDNA synthesis with a tag substance, restriction enzymes, and a high-affinity substance, or using markers on both primers, a second PCR after cDNA recovery, or cutting out the gel to litigate and clone in E. Coli as taught by Belyavsky et al. because Belyavsky et al. teaches a method to detect mRNA sequences with an increase of sensitivity and for unambiguous identification of individual fragments of cDNA (Column 3, lines 45-50). The ordinary artisan would use the cDNA fragmenting and cloning technique taught by Belyavsky et al. because Belyavsky et al. teaches the intensity of the signal from each fragment of cDNA varies dependent on the proportion of mRNA in the different cells therefore this method allows for the increased sensitivity of detecting cDNA fragments by amplifying by means of restriction and cloning (Column 3, lines 50-65).

Response to Arguments

The reply asserts the 103 rejection failed to teach removing rRNA to obtain mRNA as the newly amended claim is drawn (p. 10 2nd full paragraph). The response has been thoroughly reviewed but is not found persuasive. The combination of Wendisch et al., and Murphy et al. teaches the removing rRNA prior to mRNA polyadenation in order to provide enriched mRNA which has a polyA tail.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Katherine Salmon whose telephone number is (571) 272-3316. The examiner can normally be reached on Monday-Friday 8AM-430PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Katherine Salmon
Examiner
Art Unit 1634

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PRIMARY EXAMINER